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Docket Number: P-LG 4878

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of	Examiner: Jeffrey N. FREDMAN
PADGETT et al.	Group Art Unit: 1634
Serial No.: 10/066,390	I hereby certify that this correspondence is being facsimile transmitted to the USPTO number 703-872-9306 on December 23, 2003 by
Filed: February 2, 2002	
For: A Method of Increasing Complementarity in a Heteroduplex	John E. Tarcza Reg. No. 33,638

RESPONSE TO REQUIREMENT FOR RESTRICTION

Mail Stop Non-Fee Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

December 23, 2003

Dear Sir:

In response to the Restriction Requirement mailed November 28, 2003, Applicant hereby elects group I, which includes claims 1-63, for examination on the merits.

Amendments to the claims are reflected in the listing of claims, which begins on page 2 of this paper.

Remarks/Arguments begin on page 16 of this paper.

AMENDMENTS TO THE CLAIMS;

This listing of claims will replace all prior versions and listing of the claims in the application:

LISTING OF THE CLAIMS:

Claim 1. (original) An in vitro method of making sequence variants from at least one heteroduplex polynucleotide where said heteroduplex has at least two non-complementary nucleotide base pairs, said method comprising:

a. preparing at least one heteroduplex polynucleotide;

b. combining said heteroduplex polynucleotide with an effective amount of CEL I, T4 DNA polymerase, and T4 DNA ligase; and

c. allowing sufficient time for the percentage of complementarity to increase, wherein one or more variants are made.

Claim 2. (original) An in vitro method of making sequence variants from at least one heteroduplex polynucleotide wherein said heteroduplex has at least two non-complementary nucleotide base pairs, said method comprising:

a. preparing at least one heteroduplex polynucleotide;

b. combining said heteroduplex polynucleotide with an effective amount of an agent or agents with exonuclease activity, polymerase activity and strand cleavage activity; and

c. allowing sufficient time for the percentage of complementarity to increase, wherein at least one or more variants are made.

Claim 3. (original) The method of claim 2 wherein said heteroduplex polynucleotide is circular.

Claim 4. (original) The method of claim 2 wherein said heteroduplex polynucleotide is linear.

Claim 5. (original) The method of claim 3 or 4 wherein said heteroduplex polynucleotide is a replicon.

Claim 6. (original) The method of claim 2 wherein said variants have different amounts of complementarity.

Claim 7. (original) The method of claim 2 wherein said agents having exonuclease activity, polymerase activity, and strand cleavage activity are added sequentially.

Claim 8. (original) The method of claim 2 wherein said agents having exonuclease activity, polymerase activity, and strand cleavage activity are added concurrently.

Claim 9. (original) The method of claim 2 in step (b) further comprising ligase activity.

Claim 10. (original) The method of claim 2 further comprising a step of, (d) adding a ligase.

Claim 11. (original) The method of claim 2 wherein said agents having exonuclease activity, polymerase activity, ligase activity, and strand cleavage activity are added sequentially.

Claim 12. (original) The method of claim 2 wherein said agents having exonuclease activity, polymerase activity, ligase activity, and strand cleavage activity are added concurrently.

Claim 13. (original) The method of claim 9 wherein said ligase is T4 DNA ligase, E. coli DNA ligase, or Taq DNA ligase.

Claim 14. (original) The method of claim 2 wherein said agent with strand cleavage activity is an enzyme.

Claim 15. (original) The method of claim 2 wherein said agent with strand cleavage activity is a mismatch endonuclease.

Claim 16. (original) The method of claim 2 wherein said agent with strand cleavage

activity is selected from the group consisting of CEL I, T4 endonuclease VII, T7 endonuclease I, S1 nuclease, BAL-31 nuclease, FEN1, cleavase, pancreatic DNase I, SP nuclease, mung bean nuclease, and nuclease P1.

Claim 17. (original) The method of claim 2 wherein said agent with strand cleavage activity is a chemical.

Claim 18. (original) The method of claim 2 wherein said agent with strand cleavage activity is selected from the group consisting of potassium permanganate, tetraethylammonium acetate, sterically bulky photoactivatable DNA intercalators, [Rh(bpy)2(chrysi)]3+, osmium tetroxide with piperidine, and hydroxylamine with piperidine.

Claim 19. (original) The method of claim 2 wherein said agent with strand cleavage activity is ionizing radiation, or kinetic radiation.

Claim 20. (original) The method of claim 2 wherein said agent with polymerase activity is T4 DNA polymerase.

Claim 21. (original) The method of claim 2 wherein said agent with polymerase activity is T7 DNA polymerase.

Claim 22. (original) The method of claim 2 wherein said agent with both polymerase activity and 3' to 5' exonuclease activity is T4 DNA polymerase, T7 DNA polymerase, E. coli Pol 1, or Pfu DNA polymerase.

Claim 23. (original) The method of claim 2 wherein said agent with both polymerase activity and 5' to 3' exonuclease activity is E. coli Pol 1.

Claim 24. (original) The method of claim 2 wherein said effective amount of strand cleavage activity, and exonuclease activity/polymerase activity and ligase activity are provided by CEL I, T4 DNA polymerase, and T4 DNA ligase.

Claim 25. (original) The method of claim 2 wherein said effective amount of strand cleavage activity, and exonuclease activity/polymerase activity and ligase activity are provided by CEL I, T7 DNA polymerase, and T4 DNA ligase.

Claim 26. (original) The method of claim 2 wherein an effective amount of strand cleavage activity, and exonuclease activity/polymerase activity and ligase activity are provided by T4 endonuclease VII, T4 DNA polymerase, and T4 DNA ligase.

Claim 27. (original) An in vitro method of increasing diversity in a population of sequences, comprising: preparing at least one heteroduplex polynucleotide; combining said heteroduplex polynucleotide with an effective amount of an agent or agents with 3' to 5'

exonuclease activity, polymerase activity and strand cleavage activity; and allowing sufficient time for the percentage of complementarity to increase, wherein diversity in the population is increased.

Claim 28. (original) The method of claim 27 wherein said heteroduplex polynucleotide is circular.

Claim 29. (original) The method of claim 27 wherein said heteroduplex polynucleotide is linear.

Claim 30. (original) The method of claim 3 or 4 wherein said heteroduplex polynucleotide is a replicon.

Claim 31. (original) The method of claim 27 wherein said variants have different amounts of complementarity.

Claim 32. (original) The method of claim 27 wherein said enzymes having 3' to 5' exonuclease activity, polymerase activity, and strand cleavage activity are added sequentially.

Claim 33. (original) The method of claim 27 wherein said enzymes having 3' to 5' exonuclease activity, polymerase activity, and strand cleavage activity are added at the same

time.

Claim 34. (original) The method of claim 27 further comprising adding a ligase.

Claim 35. (original) The method of claim 9 wherein said ligase is T4 DNA ligase, E. coli DNA ligase, or Taq DNA ligase.

Claim 36. (original) The method of claim 27 wherein said agent with strand cleavage activity is an enzyme.

Claim 37. (original) The method of claim 27 wherein said agent with strand cleavage activity is a mismatch endonuclease.

Claim 38. (original) The method of claim 27 wherein said agent with strand cleavage activity is selected from the group consisting of CEL I, T4 endonuclease VII, T7 endonuclease I, S1 nuclease, BAL-31 nuclease, FEN1, cleavase, pancreatic DNase I, SP nuclease, mung bean nuclease, nuclease P1.

Claim 39. (original) The method of claim 27 wherein said agent with strand cleavage activity is a chemical.

Claim 40. (original) The method of claim 27 wherein said agent with strand cleavage

activity is selected from the group consisting of potassium permanganate, tetraethylammonium acetate, sterically bulky photoactivatable DNA intercalators, [Rh(bpy)2(chrysi)]3+, osmium tetroxide with piperidine, and hydroxylamine with piperidine.

Claim 41. (original) The method of claim 27 wherein said agent with strand cleavage activity is ionizing radiation, or kinetic radiation.

Claim 42. (original) The method of claim 27 wherein said agent with polymerase activity is T4 DNA polymerase.

Claim 43. (original) The method of claim 27 wherein said agent with polymerase activity is T7 DNA polymerase.

Claim 44. (original) The method of claim 27 wherein said agent with both polymerase activity and 3' to 5' exonuclease activity is T4 DNA polymerase, T7 DNA polymerase, E. coli Pol 1, or Pfu DNA polymerase.

Claim 45. (original) The method of claim 27 wherein said agent with both polymerase activity and 5' to 3' exonuclease activity is E. coli Pol 1.

Claim 46. (original) The method of claim 27 wherein said effective amount of strand

cleavage activity, exonuclease activity/polymerase activity and ligase activity are provided by CEL I, T4 DNA polymerase, and T4 DNA ligase respectively.

Claim 47. (original) The method of claim 27 wherein said effective amount of strand cleavage activity, and exonuclease activity/polymerase activity and ligase activity are provided by CEL I, T7 DNA polymerase, and T4 DNA ligase respectively.

Claim 48. (original) The method of claim 27 wherein said effective amount of strand cleavage activity, and exonuclease activity/polymerase activity and ligase activity are provided by CEL I, T7 DNA polymerase, and T4 DNA ligase respectively.

Claim 49. (original) The method of claim 27 wherein an effective amount of strand cleavage activity, and exonuclease activity/polymerase activity and ligase activity are provided by T4 endonuclease VII, T4 DNA polymerase, and T4 DNA ligase respectively.

Claim 50. (original) An in vitro method of increasing diversity in a population of sequences, comprising:

a. preparing at least one heteroduplex polynucleotide;

b. combining said heteroduplex polynucleotide with an effective amount of CEL I, T4 DNA polymerase, and T4 DNA ligase; and

c. allowing sufficient time for the percentage of complementarity to increase, wherein diversity in the population is increased.

Claim 51. (original) A method of obtaining a polynucleotide encoding a desired functional property, comprising:

a. preparing at least one heteroduplex polynucleotide;

b. combining said heteroduplex polynucleotide with an effective amount of an agent or agents with exonuclease activity, polymerase activity, and strand cleavage activity;

c. allowing sufficient time for the percentage of complementarity between strands of the heteroduplex polynucleotide to increase, wherein diversity in the population is increased; and

d. screening or selecting a population of variants for the desired functional property.

Claim 52. (original) A method of obtaining a polynucleotide encoding a desired functional property, comprising:

a. preparing at least one heteroduplex polynucleotide;

b. combining said heteroduplex polynucleotide with an effective amount of an agent or agents with exonuclease activity, polymerase activity, and strand cleavage activity;

c. allowing sufficient time for the percentage of complementarity between strands of the heteroduplex polynucleotide to increase, wherein diversity in the population is increased;

d. converting DNA to RNA; and

e. screening or selecting a population of ribonucleic acid variants for the desired functional property.

Claim 53. (original) A method of obtaining a polypeptide having a desired functional property, comprising:

a. preparing at least one heteroduplex polynucleotide;

b. combining said heteroduplex polynucleotide with an effective amount of an agent or agents with exonuclease activity, polymerase activity and strand cleavage activity;

c. allowing sufficient time for the percentage of complementarity between strands of said heteroduplex polynucleotide to increase,

d. converting said heteroduplex polynucleotide to RNA, and said RNA to a polypeptide; and

e. and screening or selecting a population of polypeptide variants for said desired functional property.

Claim 54. (original) A method of obtaining a polynucleotide encoding a desired functional property, comprising:

a. preparing at least one heteroduplex polynucleotide;

b. combining said heteroduplex polynucleotide with an effective amount of an agent or agents with exonuclease activity, polymerase activity and strand cleavage activity;

c. allowing sufficient time for the percentage of complementarity between strands of said heteroduplex polynucleotide to increase,

d. screening or selecting for a population of variants having a desired functional property;

e. denaturing said population of variants to obtain single strand polynucleotides;

f. annealing said single strand polynucleotides to form at least one second heteroduplex polynucleotide;

g. combining said second heteroduplex polynucleotide with an effective amount of an agent or agents with exonuclease activity, polymerase activity and strand cleavage activity; and

h. allowing sufficient time for the percentage of complementarity between strands of the heteroduplex polynucleotide to increase.

Claim 55. (original) The method of claim 54 wherein said heteroduplex polynucleotide is greater than 95% identical.

Claim 56. (original) The method of claim 54 wherein said heteroduplex polynucleotide is about 95% identical.

Claim 57. (original) The method of claim 54 wherein said heteroduplex polynucleotide is about 90% identical.

Claim 58. (original) The method of claim 54 wherein said heteroduplex polynucleotide is about 85% identical.

Claim 59. (original) The method of claim 54 wherein said heteroduplex polynucleotide is about 80% identical.

Claim 60. (original) The method of claim 54 wherein said heteroduplex polynucleotide is about 75% identical.

Claim 61. (original) The method of claim 2 wherein the heteroduplex polynucleotide is about 1000 Kb.

Claim 62. (original) The method of claim 2 wherein the heteroduplex polynucleotide is about 10,000 Kb.

Claim 63. (original) The method of claim 2 wherein the heteroduplex polynucleotide is about 100,000 Kb.

Claim 64. (canceled) A kit used for increasing diversity in a population of sequences, comprising: preparing at least one heteroduplex polynucleotide; combining said heteroduplex polynucleotide with an effective amount of an agent or agents with 3' to 5'

exonuclease activity, polymerase activity and strand cleavage activity; and allowing sufficient time for the percentage of complementarity to increase, wherein diversity in the population is increased.

Claim 65. (canceled) The kit of claim 64 further comprising having a ligase activity.

REMARKS/ARGUMENTS

In response to the Restriction Requirement mailed November 28, 2003, Applicants elect group I, which includes claims 1-63, for examination on the merits.

To avoid the restriction requirement, applicants have, canceled non-elected claims 64-65, without prejudice to the filing of a continuating or divisional application with the same claims. Therefore, claims 1-63 are now pending in the application and an action on the merits is requested.

The commissioner hereby is authorized to charge payment of any fees under 37 CFR § 1.17, which may become due in connection with the instant application or credit any overpayment to Deposit Account No.500933.

Respectfully submitted,

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